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A Cost-Utility Analysis Comparing Standard Axillary Lymph Node Dissection with Sentinel Lymph Node Biopsy in Patients with Early Stage Breast Cancer in Thailand

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ABSTRACT

Objectives: In Thailand, axillary lymph node dissection (ALND) is the dominant form of treatment for breast cancer, even though the treatment often leaves patients with some degree of arm morbidity. Sentinel lymph node biopsy (SNB) is widely accepted globally as a preferable alternative procedure because of its lower rates of associated morbidity. This study compared the cost-utility of SNB and ALND in patients with early stage breast cancer in Thailand. **Methods:** A decision tree with a 5-year time horizon was developed. Outcomes that were relevant to SNB and ALND were included, along with locoregional recurrence of cancer and lymphedema scenarios. The model parameters were derived from a meta-analysis of international clinical trials and other relevant literature. The resources and cost data were derived from the medical records of tertiary hospitals. Health utilities were measured by using the standard gamble technique. A sensitivity analysis was performed using a set of plausible parameters. **Results:** The incremental cost-effectiveness ratio (ICER) in the base-case analysis showed that SNB was more cost-effective than ALND. ICERs were −275,140 and −470,600 Thailand baht/quality-adjusted life-year gained from the provider perspective and the societal perspective, respectively. The most sensitive parameter was the utility score of patients with early stage breast cancer who had received breast-conserving therapy with lymphedema; the sensitivity and specificity of SNB had no impact on the ICER. **Conclusions:** The study confirmed that SNB was an economically viable alternative treatment to ALND. In developing countries, where resources are limited, nationwide implementation of SNB warrants widespread support from relevant stakeholders, including medical personnel and policymakers.

Keywords: axillary lymph node dissection, breast cancer, cost-utility analysis, sentinel lymph node biopsy.

Introduction

Over the last 10 years, the incidence of breast cancer in Thailand has increased significantly. The age-standardized rate for breast cancer has risen from 20.4 per 100,000 in 2003 to 25.6 per 100,000 in 2006. Today, 29,167 cases are diagnosed each year [1], making it the leading cancer in women in Thailand. Advancements in cancer care that have occurred over the last 10 years, particularly the multidisciplinary approach that has resulted from collaboration between surgeons, oncologists, and radiologists, has resulted in a dramatic improvement in both the survival rate and the quality of life of patients with breast cancer. Although advanced adjuvant chemo-radiation plays an important role in cancer care, surgery is still the main treatment option for local control of disease. Because the breast lymphatic system is drained through axillary lymph nodes, axillary lymph node dissection (ALND) has become a standard treatment for both cancer staging and the controlling of local recurrence (LR). Axillary recurrence decreases the 5-year survival rate of patients with breast cancer by approximately 28% to 40% [2,3]. However, ALND causes arm morbidity in around 20% of the patients, including symptoms such as frozen shoulder, armedema, and lymphagitis [4]. Following the introduction of screening mammograms, the number of stage breast cancer cases that exhibit axillary metastasis has decreased significantly because of earlier detection [5]. Many studies [6,7] report that as many as 70% to 80% of patients with early stage breast cancer show no axillary lymph nodes metastasis. For patients who show no palpable axillary lymph node, sentinel lymph node biopsy (SNB) is conducted to identify the first drainage lymph node, which can prevent the need for ALND. SNB has been widely accepted worldwide [8] as a comparative procedure to ALND that can identify early metastasis in patients with early stage breast cancer who have a tumor smaller than 5 cm and a clinically nonpalpable axillary lymph node. The procedure has

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been shown to reduce the risk of many short- and long-term complications associated with ALND, including long hospital stays, infection, lymphedema, and frozen shoulder. For instance, Kell et al. [9] reported a 70% reduction in the rate of lymphedema and a 75% reduction in the rate of arm numbness for patients who underwent SNB as opposed to ALND. Veronesi et al. [10] also found that SNB and ALND resulted in a similar 10-year survival, LR, and metastasis rates.

Although ALND causes higher levels of morbidity than does SNB, ALND is still the standard procedure for patients with breast cancer in Thailand, due to a lack of both trained personnel and facilities that are necessary to implement SNB nationwide. No economic evaluation has yet been undertaken in any developing country setting to compare the cost-effectiveness of ALND and SNB in terms of cost, treatment outcome, and complications. This study aimed to address this gap in the data by evaluating the cost-utility of SNB compared with ALND in patients with early stage breast cancer in Thailand. The results will help health care providers and policymakers decide whether to put SNB into clinical practice throughout the country.

Methods

Overview

In Thailand, all patients who are diagnosed with early stage breast cancer and who have no palpable axillary lymph nodes undergo either a mastectomy or breast-conserving therapy (BCT); these surgical treatment options are conducted with either SNB or ALND, depending on the surgeon's preference. ALND is far more common in standard treatment than is SNB, which is currently performed only in a few university and tertiary hospitals throughout Thailand. Following SNB or ALNB, chemo-radiation is usually provided, followed by a 5-year hormonal treatment.

To compare the economic value of SNB with ALND, we conducted an evaluation using a hypothetical cohort of women aged 50 years who were diagnosed with early stage breast cancer and had clinically nonpalpable axillary lymph nodes. We chose to focus on postmenopausal women aged 50 years because this is the age at which breast cancer incidence peaks in Thai women [1]. All costs and outcomes after the first year were discounted at a rate of 3% per annum, as recommended by Thailand's health technology assessment guidelines [11].

Design of analysis model

The study was based on a decision analytic model that compared the cost and utility of ALND with those of SNB in patients with early stage breast cancer in Thailand from societal and provider perspectives. We generated a decision tree with a 5-year time horizon (Fig. 1) that covered all relevant outcomes, including lymphedema and locoregional recurrence rates. All patients were postmenopausal and underwent BCT and either axillary dissection or SNB. For each procedure, the pathology results may be positive (true positive, false negative) or negative (true negative, false positive). Some patients who undergo SNB may later undergo ALND as well, in cases in which the axillary lymph nodes were found to have metastasized. There are two main techniques used to identify the sentinel lymph node in SNB—either a blue dye or a radioactive substance is injected near to the tumor site. In this study, only the blue dye technique was included in the analysis because this is the procedure that is commonly used in the Thai setting. Given the lack of frozen section data in Thailand, we assumed the frozen section data from the diagnosis stage of SNB, which is conducted intraoperationally, to be 100% accurate. Although sensitivity and specificity of SNB were reported from the final histopathology examination, we conducted sensitivity analysis on these two parameters to minimize these parameters and frozen section uncertainty. Another model assumption was that all SNBs were performed by experienced surgeons who had passed the "learning curve" period. After both SNB and ALND, there is a risk that patients may experience lymphedema in the second and third years after treatment. In the fourth and fifth years, patients experience one of three possible outcomes—LR, regional recurrence (RR), or no locoregional recurrence. For those who experience LR, a mastectomy is usually conducted, either with or without axillary dissection; for those who experience RR, axillary clearance is usually conducted. In both recurrence groups, there is a risk that patients might experience lymphedema after the second surgery. All patients received chemotherapy and radiation after treatment, as per standard guidelines.

Final health states represent the outcomes measurement in most clinical trials, which use the presence of lymphedema, LR, and RR in the arm (or absence thereof). The distance metastasis rate in patients with early stage breast cancer is predominantly dependent on initial staging, which is usually similar in both arms; therefore, we did not assess this in the analysis.

Model parameters

Clinical parameters were decided on the basis of an extensive search of the published data. They are summarized in Table 1. The prevalence of axillary lymph node metastasis in 2-cm tumors was 31.5%, which increased in-line with tumor size. The sensitivity and specificity of SNB were derived from a meta-analysis of six randomized controlled trials (RCTs) [15–20], which compared SNB and ALND in patients with early stage breast cancer. The locoregional recurrences of SNB were derived from a meta-analysis of five RCTs [10,15,22,23], while the recurrence rate for ALND was derived from a single RCT [24] because no other published data were available. Because many of the clinical trials that examine lymphedema measurements use many different methods, we used data only from one RCT (NSABP B-32) to avoid confusion. The NSABP B-32 trial measured the lymphedema rates for both SNB and ALND patients using the water displacement method, which is recognized as the most reliable method for assessing lymphedema rates [26]. We analyzed the lymphedema rate as part of our sensitivity analysis.

Utility

Quality-adjusted life-years (QALYs) were derived from the patients' life-years and utility scores. Utility was measured using the standard gamble technique in 110 healthy Thai women aged 26 to 60 years because women in these ages can develop breast cancer. All hypothetical health states were developed on the basis of evidence from the literature review and expert opinions. Patient-reported outcomes [28,29] related to health quality of life in patients with breast cancer were reviewed and modified so that they were appropriate for the Thai context. Although the cognitive interview included questions related to sexual well-being, these responses were excluded from health state description because they were deemed irrelevant. Content validation was conducted by three medical professionals who specialized in caring for patients with breast cancer and five patients with breast cancer. The construct validity was proven by the statistical difference between better health states and worse health states (such as early stage breast cancer and recurrence of breast cancer). The six health states were as follows: 1) early stage breast cancer treated with BCT, with no recurrence, but with lymphedema; 2) early stage breast cancer treated with BCT, with no recurrence and without lymphedema; 3) LR of breast cancer, with lymphedema; 4) LR of breast cancer without lymphedema; 5) RR of breast cancer, with lymphedema; and 6) RR of breast cancer without lymphedema. Patients who experienced LR were treated with a mastectomy with axillary dissection, whereas those experiencing RR were treated with only additional axillary dissection. We assumed that the outcomes of

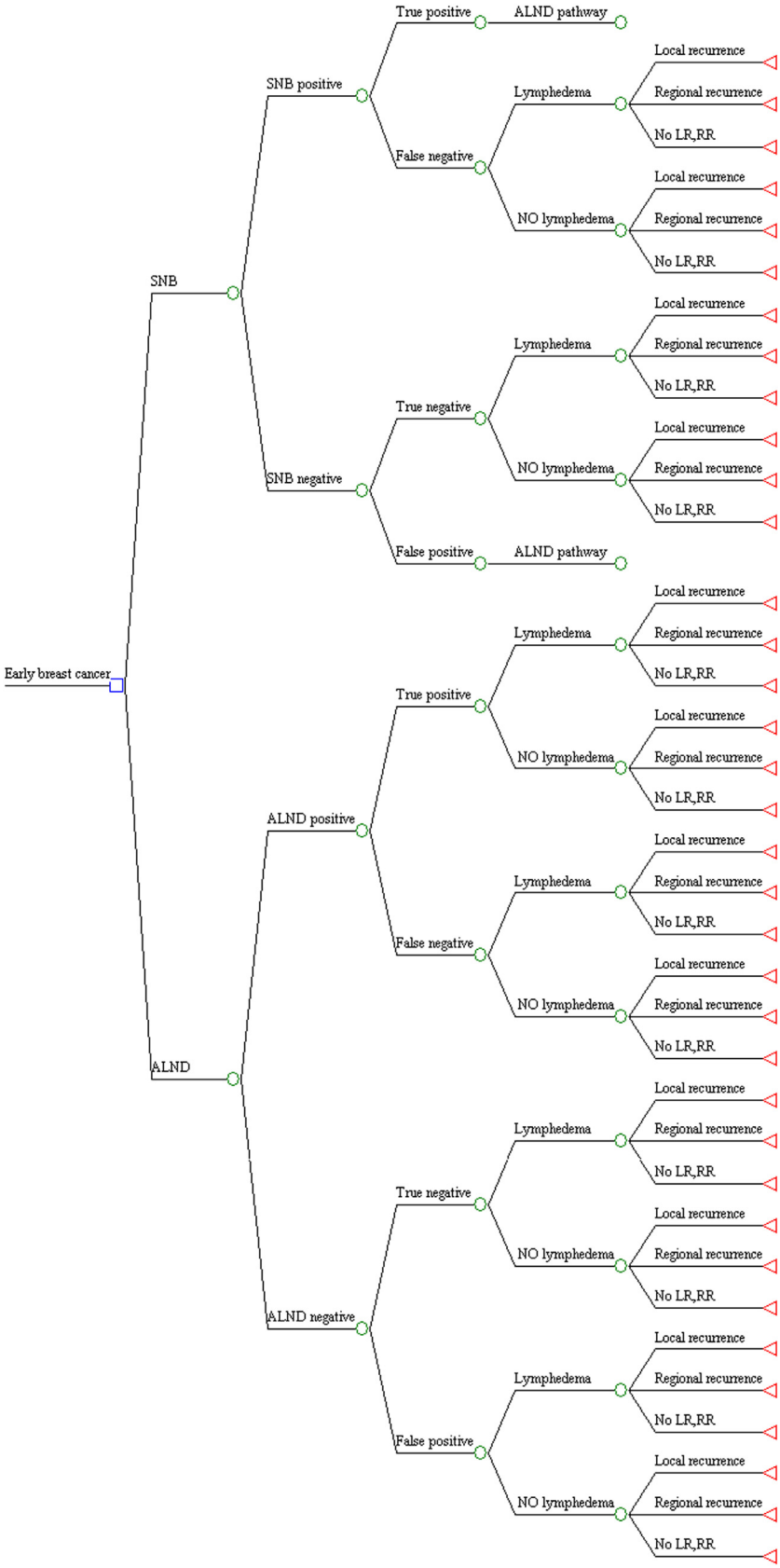

Fig. 1 – Decision tree. ALND, axillary lymph node biopsy; LR, local recurrence; RR regional recurrence; SNB, sentinel lymph node biopsy.

Table 1 – Model parameters and data sources.

Parameter	Distribution	Mean	Standard error	Data source
Probability of axillary metastasis in 2-cm tumors	Beta	0.315	0.018	[12–14]
SNB				
Sensitivity	Beta	0.902	0.017	[15–20]
Specificity	Beta	1.0	0	[15–20]
ALND				
Sensitivity	Beta	0.304	0.038	[21]
Specificity	Beta	0.988	0.004	[21]
Probability of local recurrence				
SNB negative and no metastasis lymph node (true negative)	Beta	0.022	0.003	[10,15,22,23]
SNB negative and metastasis lymph node (false negative)	Beta	0.019	0.006	[24]
ALND with no metastasis lymph node	Beta	0.014	0.006	[10,15,22,23]
ALND with metastasis lymph node	Beta	0.036	0.009	[24]
Probability of regional recurrence				
SNB negative and no metastasis lymph node (true negative)	Beta	0.004	0.002	[10,15,22,23,25]
SNB negative and metastasis lymph node (false negative)	Beta	0.009	0.005	[24]
ALND with no metastasis lymph node	Beta	0.004	0.001	[10,15,22,23,25]
ALND with metastasis lymph node	Beta	0.005	0.003	[24]
Probability of lymphedema				
SNB	Beta	0.117	0.011	[26]
ALND	Beta	0.276	0.013	[26]
Utilities for health states*				
Early stage breast cancer status after BCT	Beta	0.76	0.04	
Early stage breast cancer status after BCT with lymphedema	Beta	0.59	0.04	
Advanced stage breast cancer with regional recurrence	Dirichlet	0.60	0.04	
Advanced stage breast cancer with regional recurrence and lymphedema	Dirichlet	0.45	0.03	
Advanced stage breast cancer with local recurrence	Dirichlet	0.61	0.03	
Advanced stage breast cancer with local recurrence and lymphedema	Dirichlet	0.39	0.03	
Cost				
Direct medical cost†				
First-year cost of SNB	Gamma	39,673.80	2,561.30	
First-year cost of SNB and ALND	Gamma	61,100.37	14,947.61	
First-year cost of ALND	Gamma	47,737.25	3,794.58	
Cost of follow-up of SNB per year	Gamma	3,207.51	47.99	
Cost of follow-up of SNB and ALND per year	Gamma	5,013.62	210.05	
Cost of follow-up of ALND per year	Gamma	7,954.54	325.54	
Operation after local recurrence (2 y)	Gamma	44,022.99	44,022.99	
Operation after regional recurrence (2 y)	Gamma	3,9254.19	3,9254.19	
Radiation cost in early stage breast cancer (5 y)	Gamma	51,126.51	51,126.51	
Chemo-radiation cost for recurring breast cancer (3 y)	Gamma	11,7285.6	11,7285.6	
Lymphedema care cost (4 y)	Gamma	102,084.95	102,084.95	
Lymphedema care cost (2 y)	Gamma	82,966.29	82,966.29	
Direct nonmedical cost				
Cost of travel	Gamma	142.55	11.60	[27]
Cost of food	Gamma	52.51	5.35	[27]
Indirect cost				
Cost of productivity loss of patient per day	Gamma	80.29	11.34	[27]
Cost of productivity loss of one relative per day	Gamma	95.51	35.41	[27]

ALND, axillary lymph node dissection; BCT, breast-conserving therapy; SNB, sentinel lymph node biopsy.
* Data source: Interview (standard gamble technique).
† Data source: Hospital databases

both the SNB group and the ALND group would show similar clinical presentation and would share the same health states given the similar clinical progression of both procedures but would differ in the occurrence rate. The utility data are presented in Table 1.

Cost

Both the societal and health care provider perspectives were examined in this analysis. The cost used in the societal perspective was composed of direct medical costs and direct nonmedical costs, whereas the cost used in the provider perspective included only direct medical costs. Direct medical costs were grouped into three categories—surgical procedures, lymphedema care, and radiation and chemotherapy. Direct medical costs of each procedure comprised operation costs, anesthesia care costs, hospitalization costs, and related investigation and medication costs. Lymphedema care costs comprised physiotherapy care costs and medication costs. Radiation costs comprised

radiation therapy costs and medication and investigation costs. Number of resources used for all cost items and their charge were derived from the financial databases of the university hospital and the national cancer center. All charges were converted to costs using the cost to charge ratio reported by Riewpaiboon [27]. Chemotherapy costs were taken from Supakul et al. [31]. Direct nonmedical costs, which comprised patient expenses for food, transportation, and costs arising from relative productivity loss during hospitalization and outpatient visits, were derived from standard cost lists for health technology assessment [27]. Follow-up schedules and investigations were in line with those outlined in international guidelines [32]. Costs of lymphedema comprised first-year procedure costs and follow-up costs per year for 4 or 5 years of radiation treatment. For patients who experienced arm lymphedema in the second year, additional lymphedema care costs were calculated for 4 years. If patients had LR or RR, costs included the operation in the first year plus costs associated with two follow-up years and costs of the second operation and chemo-radiation. For patients undergoing a second procedure and who experienced lymphedema, costs included lymphedema care for 2 years. We excluded the cost of chemotherapy and hormonal therapy after the first treatment because we assumed that all patients received the same treatment and so the cost would not affect the results. All costs were adjusted for inflation to the year 2012 by applying the Thai consumer price index [30].

Uncertainty Analysis

A one-way sensitivity analysis was performed on all relevant parameters, including the prevalence of axillary metastasis, sensitivity and specificity of SNB, cost of each procedure, and utility score. The value of each parameter was tested within a plausible range of 95% confidence interval (CI) or 10th and 90th percentile. A threshold analysis was undertaken on relevant parameters at a willingness-to-pay (WTP) value of 120,000 Thai baht (THB) per QALY gained, as recommended by the Health Economic Working Group under the Subcommittee for Development of the National List of Essential Drugs. A probabilistic sensitivity analysis using the Monte-Carlo stimulation with 1000 iterations was undertaken to test the uncertainty of the model. A gamma distribution was used for cost, while the beta distribution and the dirichlet distribution was used for probability and utility parameters, respectively. Because cost of operation after recurrence, lymphedema care cost, and radiation cost came from the reimbursement list, values for standard error for these were not available. We used standard error equal to mean in sensitivity analysis. A cost-effectiveness acceptability curve was also presented.

Results

The base-case analysis of the cost utility of SNB and ALND in patients with early stage breast cancer found that SNB cost less than ALND but resulted in higher QALYs. The incremental cost-effectiveness ratios (ICERs) of SNB compared with those of ALND were −275,140 THB/QALY gained from the provider perspective and −470,600 THB/QALY gained from the societal perspective (see Table 2).

One-Way Sensitivity Analysis

Our one-way sensitivity analysis (Fig. 2) showed that the utility score of early stage breast cancer, post-BCT patients with lymphedema was the most sensitive parameter, in which a range of 95% CI in the parameter resulted in an ICER range of −145% to 316%. In contrast, the probability of a true positive outcome (sensitivity) had a minimal effect on ICER for both ALND and SNB. Tumor mass determines the prevalence of axillary metastasis; given that, a threshold analysis was performed to explore the effect of the axillary metastasis rate on the value for money of SNB. The results showed that at a WTP value of 120,000 THB/QALY gained, SNB was superior to ALND, even when the rate of axillary metastasis changed from 0% to 85%. The axillary metastasis rate in early stage breast cancer cases, in which the tumor is smaller than 5 cm, was found to be approximately 49% to 58% [12–14]. This means that SNB is statistically more cost-effective than ALND for early stage breast cancer treatment. Given that some model parameters obtained from international studies are generally more accurate than parameters garnered from clinical practice, the sensitivity and specificity of SNB were also tested. The results from the one-way sensitivity analysis showed that both parameters were less sensitive to ICER change and that SNB was still more cost-effective even when the sensitivity and specificity of the test decreased. The lymphedema rate after ALND was tested because the severity of lymphedema in post-ALND patients can vary widely, and many patients with a mild form of lymphedema may not require treatment. We found that ALND was the more cost-effective treatment option, when fewer than 10% of the patients developed lymphedema; however, this was not verifiable in the clinical setting, in which more than 10% of the patients who had ALND develop lymphedema. Moreover, direct medical cost applied in this study did not include the cost that occurred during the learning curve of SNB; however, in one-way sensitivity analysis, ICER showed minimal change when the direct medical cost of SNB in the first year varied between 10th and 90th percentile.

Probabilistic Sensitivity Analysis

The probabilistic sensitivity analysis showed that SNB is more cost-effective than ALND for all WTP values (Fig. 3). At a WTP value of 120,000 THB, the probability of SNB being cost-effective was 77.5% while the probability of ALND being cost-effective was 22.5%.

Discussion

Our cost-utility analysis was based on a 5-year decision tree model that compared the cost-effectiveness of ALND with SNB treatments for patients with early stage breast cancer in Thailand from both the provider and societal perspectives. SNB was found to be cost saving from both perspectives, giving an ICER of −275,140 THB/QALY gained from the provider perspective and −470,600 THB/QALY gained from the societal perspective. At Thailand's ceiling threshold of 120,000 THB/QALY gained, the probability that SNB would be cost-effective in patients with early stage breast cancer was found to be 77.5%. Some model parameters were derived from international studies, in which breast cancer tends to be diagnosed at an earlier stage than in Thailand, and so tumors tend to be smaller and the risk of axillary metastasis is correspondingly lower. Despite this, our threshold analysis still confirmed SNB to be the most cost-effective option, despite the significantly high risk of axillary metastasis (85%). In clinical practice, however, SNB was not recommended for patients with a tumor larger than 5 cm because of its high false-negative rate with tumors of that size.

In Thailand, most patients with breast cancer undergo a mastectomy, in contrast to most international contexts that have been studied, in which BCT is the most common surgical treatment. Many studies [33,34] have shown that the outcomes of mastectomy are comparable with those of BCT in terms of LR and survival rate. However, because of criteria and follow-up period limitations in previous studies, no definitive evidence has yet

Table 2 – Cost-effectiveness of SNB and ALND in provider and societal perspective.

Treatment	QALYs	Cost (THB)		ICER	
		Provider	Societal	Provider	Societal
ALND*	3.385	152,212	215,473		
SNB*	3.431	139,552	193,820	−275,140	−470,600

ALND, axillary lymph node dissection; ICER, incremental cost-effectiveness ratio; QALYs, quality-adjusted life years; SNB, sentinel lymph node biopsy; THB, Thai baht.
* Excluding cost of first chemotherapy and hormonal treatment.

been established [35–37] on how the lymphedema rate differs for each procedure. However, the one-way sensitivity analysis that was conducted as part of this study on the probability of developing lymphedema revealed a range of 95% CI. The results showed a minimal change in ICER as a result of developing lymphedema, and SNB was still considered more cost-effective. The one-way sensitivity analysis of the sensitivity and specificity of SNB demonstrated that SNB was still more cost-effective than ALND.

In 2012, Verry et al. [38] compared the cost-effectiveness of SNB with that of ALND from the provider perspective using a Markov model over a 20-year period. The study parameters were mainly garnered from the Sentinel Node versus Axillary Clearance trial [18], and the utility was derived from Kanis et al. [39]. The study showed that SNB was marginally more cost-effective than ALND and indicated several sensitive parameters that affected the outcomes. The researchers highlighted the need for more reliable information on the specificity of SNB and the risk of axillary recurrence after SNB; we did not identify this need in our study. Although no relevant clinical trials have yet been conducted in Thailand from which we could derive our parameters, we ensured that the parameters were appropriate for the Thai context by deriving the utility from healthy Thai women and testing sensitive parameters through a sensitivity analysis. The most sensitive parameter that we identified in our analysis was the utility of early stage breast cancer post-BCT patients with lymphedema. Although SNB had the additional cost of pathological examination, there were studies [40,41], which compared direct medical costs between SNB and ALND in the early postoperative period, that found that SNB was cost saving and hospital stay cost was the most significant parameter. In our study, the duration of hospital stay between both groups was not much different because the patients were discharged early and had follow-up at the outpatient clinic. Because most breast cancer treatments are undertaken in outpatient clinics, we included direct nonmedical costs and examined the data from both the provider and societal perspectives. The ICER from the societal perspective was found to be nearly twice that from the provider perspective, and the cost of travel was one of the most sensitive parameters. After conducting the probabilistic sensitivity analysis with 1000 iterations in a range of probable values of total cost, health outcomes, and ICERs, the results showed that the probability of SNB being more cost-effective than ALND at different WTP values was more than 70%.

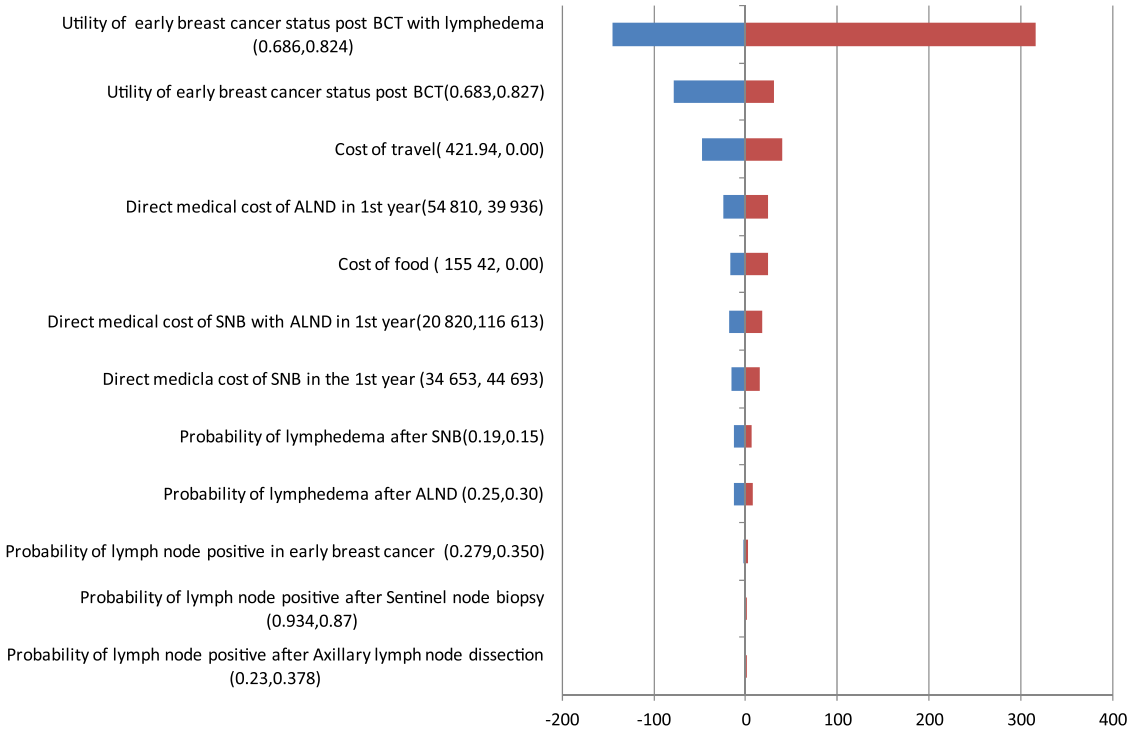

Fig. 2 – The percentage change in ICER compared with the mean ICER for each parameter. Mean ICER = −470,602.22 THB/QALY gained. ALND, axillary lymph node dissection; BCT, breast-conserving therapy; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year; SNB, sentinel lymph node biopsy; THB, Thai baht.

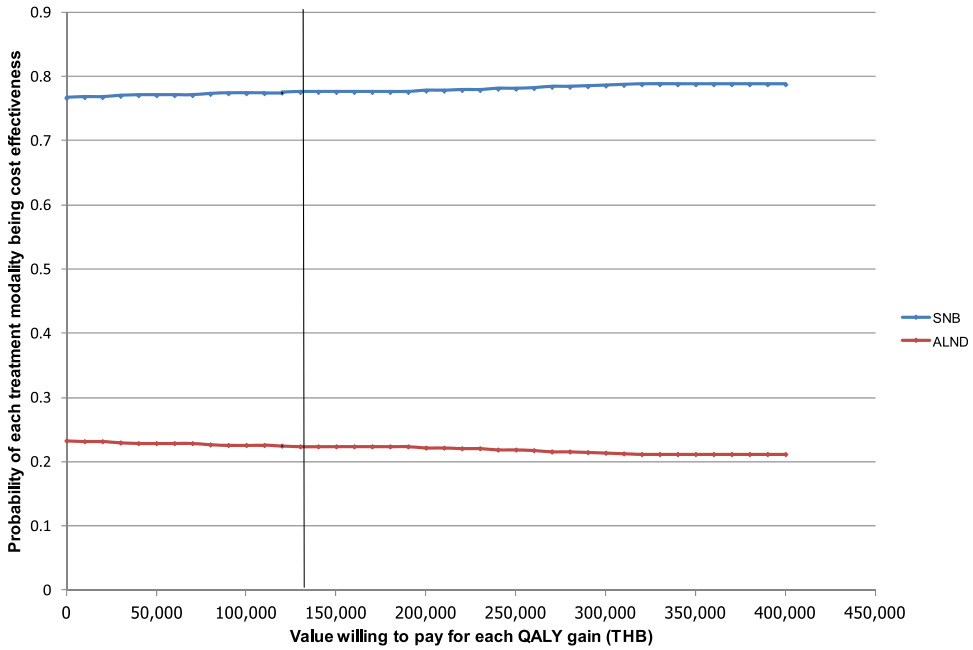

Fig. 3 – Cost-effectiveness acceptability curve. ALND, axillary lymph node dissection; QALY, quality-adjusted life-year; SNB, sentinel lymph node biopsy.

Because we used a 5-year model, our study had insufficient data to interpret the cost-utility between SNB and ALND over a lifetime. Our model aimed to evaluate the efficacy of SNB in reducing lymphedema while also giving similar LR and RR rates to ALND. Recurrence almost always occurs within 5 years after treatment, and so this model is deemed to be a good model for predicting recurrence rates. We did not include survival as an outcome because this fell outside the timescale of our model. Our assumption was in line with the data from Veronesi et al. [10], the longest follow-up clinical trial, results of which showed that mortality in early stage breast cancer was strongly predicated by initial staging and treatment and that after 10-year follow up there was no statistically significant difference in the mortality rate between SNB and ALND groups.

Conclusions

Our study demonstrated that SNB gives patients with early stage breast cancer a better quality of life and is a more cost-effective option than ALND. The results are generalizable to other Southeast-Asian countries because these countries share broadly similar living costs, cultural norms, and lifestyles to those examined in our study. Moreover, our findings make a clear case for clinicians and policymakers to provide SNB treatment nationwide to improve the standard of care for Thai patients with breast cancer.

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REFERENCES

[1] Khuhaprema T, Attasara P, Sriplug H, et al. Cancer in Thailand. Bangkok: Ministry of Public Health, 2012.
[2] Fisher B, Wolmark N, Redmond C, et al. Findings from NSABP Protocol No. B-04: comparison of radical mastectomy with alternative treatments, II: the clinical and biologic significance of medial-central breast cancers. Cancer 1981;48:1863–72.
[3] Carter CL, Allen C, Henson DE. Relation of tumor size, lymph node status, and survival in 24,740 breast cancer cases. Cancer 1989;63:181–7.
[4] Soran A, D'Angelo G, Begovic M, et al. Breast cancer-related lymphedema–what are the significant predictors and how they affect the severity of lymphedema? Breast J 2006;12:536–43.
[5] Cady B, Chung MA. Preventing invasive breast cancer: another benefit from mammographic screening. Cancer 2011;117:3064–8.
[6] Shaw JH, Rumball EM. Complications and local recurrence following lymphadenectomy. Br J Surg 1990;77:760–4.
[7] Fisher BJ, Perera FE, Cooke AL, et al. Long-term follow-up of axillary node-positive breast cancer patients receiving adjuvant tamoxifen alone: patterns of recurrence. Int J Radiat Oncol Biol Phys 1998;42:117–23.
[8] Lyman GH, Giuliano AE, Somerfield MR, et al. American Society of Clinical Oncology guideline recommendations for sentinel lymph node biopsy in early-stage breast cancer. J Clin Oncol 2005;23:7703–20.
[9] Kell MR, Burke JP, Barry M, et al. Outcome of axillary staging in early breast cancer: a meta-analysis. Breast Cancer Res Treat 2010;120:441–7.
[10] Veronesi U, Viale G, Paganelli G, et al. Sentinel lymph node biopsy in breast cancer: ten-year results of a randomized controlled study. Ann Surg 2010;251:595–600.
[11] Permsuwan U, Guntawongwan K, Buddhawongsa P. Handling time in economic evaluation studies. J Med Assoc Thai 2008;91(Suppl. 2): S53–8.
[12] Olivotto IA, Jackson JS, Mates D, et al. Prediction of axillary lymph node involvement of women with invasive breast carcinoma: a multivariate analysis. Cancer 1998;83:948–55.

[13] Coombs N, Chen W, Taylor R, et al. A decision tool for predicting sentinel node accuracy from breast tumor size and grade. Breast J 2007;13:593–8.
[14] Voogd AC, Coebergh JW, Repelaer van Driel OJ, et al. The risk of nodal metastases in breast cancer patients with clinically negative lymph nodes: a population-based analysis. Breast Cancer Res Treat 2000;62:63–9.
[15] Canavese G, Catturich A, Vecchio C, et al. Sentinel node biopsy compared with complete axillary dissection for staging early breast cancer with clinically negative lymph nodes: results of randomized trial. Ann Oncol 2009;20:1001–7.
[16] Zavagno G, Meggiolaro F, Bozza F, et al. Sentinel lymph node biopsy in breast cancer: the GIVOM experience in Veneto, Italy. Tumori 2002;88 (Suppl.):S52–4.
[17] Veronesi U, Paganelli G, Viale G, et al. A randomized comparison of sentinel-node biopsy with routine axillary dissection in breast cancer. N Engl J Med 2003;349:546–53.
[18] Gill G. Sentinel-lymph-node-based management or routine axillary clearance? One-year outcomes of sentinel node biopsy versus axillary clearance (SNAC): a randomized controlled surgical trial. Ann Surg Oncol 2009;16:266–75.
[19] Goyal A, Newcombe RG, Chhabra A, et al. Factors affecting failed localisation and false-negative rates of sentinel node biopsy in breast cancer–results of the ALMANAC validation phase. Breast Cancer Res Treat 2006;99:203–8.
[20] Krag DN, Anderson SJ, Julian TB, et al. Technical outcomes of sentinel-lymph-node resection and conventional axillary-lymph-node dissection in patients with clinically node-negative breast cancer: results from the NSABP B-32 randomised phase III trial. Lancet Oncol 2007;8:881–8.
[21] Cote RJ, Peterson HF, Chaiwun B, et al. Role of immunohistochemical detection of lymph-node metastases in management of breast cancer. International Breast Cancer Study Group. Lancet 1999;354:896–900.
[22] Krag DN, Anderson SJ, Julian TB, et al. Sentinel-lymph-node resection compared with conventional axillary-lymph-node dissection in clinically node-negative patients with breast cancer: overall survival findings from the NSABP B-32 randomised phase 3 trial. Lancet Oncol 2010;11:927–33.
[23] Zavagno G, De Salvo GL, Scalco G, et al. A randomized clinical trial on sentinel lymph node biopsy versus axillary lymph node dissection in breast cancer: results of the Sentinella/GIVOM trial. Ann Surg 2008;247:207–13.
[24] Giuliano AE, Hunt KK, Ballman KV, et al. Axillary dissection vs no axillary dissection in women with invasive breast cancer and sentinel node metastasis: a randomized clinical trial. JAMA 2011;305:569–75.
[25] Mansel RE, Fallowfield L, Kissin M, et al. Randomized multicenter trial of sentinel node biopsy versus standard axillary treatment in operable breast cancer: the ALMANAC Trial. J Natl Cancer Inst 2006;98:599–609.
[26] Ashikaga T, Krag DN, Land SR, et al. Morbidity results from the NSABP B-32 trial comparing sentinel lymph node dissection versus axillary dissection. J Surg Oncol 2010;102:111–8.
[27] Riewpaiboon A. Standard cost lists for health technology assessment. Available from: http://www.hitap.net/costingmenu/. [Accessed October 31, 2012].
[28] Brady MJ, Cella DF, Mo F, et al. Reliability and validity of the Functional Assessment of Cancer Therapy-Breast quality-of-life instrument. J Clin Oncol 1997;15:974–86.
[29] Sprangers MA, Cull A, Groenvold M, et al. The European Organization for Research and Treatment of Cancer approach to developing questionnaire modules: an update and overview. EORTC Quality of Life Study Group. Qual Life Res 1998;7:291–300.
[30] Bureau of Trade and Economic Indices, Ministry of Commerce. Report for consumer price index of Thailand, base year 2007 [database on the Internet]. Available from: http://www.indexpr.moc.go.th/price_present/TableIndexG_region.asp [Accessed October 31, 2012].
[31] Supakul S, Sooksriwong C, Chiersilpa A, et al. Cost of breast cancer treatment with adjuvant therapy in Thai women. Warasan Phesatchasat 2006;33:9–14.
[32] Khatcheressian JL, Wolff AC, Smith TJ, et al. American Society of Clinical Oncology 2006 update of the breast cancer follow-up and management guidelines in the adjuvant setting. J Clin Oncol 2006;24:5091–7.
[33] Fisher B, Jeong JH, Anderson S, et al. Twenty-five-year follow-up of a randomized trial comparing radical mastectomy, total mastectomy, and total mastectomy followed by irradiation. N Engl J Med 2002;347:567–75.
[34] Clarke M, Collins R, Darby S, et al. Effects of radiotherapy and of differences in the extent of surgery for early breast cancer on local recurrence and 15-year survival: an overview of the randomised trials. Lancet 2005;366:2087–106.
[35] Kissin MW, Querci della Rovere G, Easton D, et al. Risk of lympho-edema following the treatment of breast cancer. Br J Surg 1986;73: 580–4.
[36] Tsai RJ, Dennis LK, Lynch CF, et al. The risk of developing arm lymphedema among breast cancer survivors: a meta-analysis of treatment factors. Ann Surg Oncol 2009;16:1959–72.
[37] Nesvold IL, Dahl AA, Løkkevik E, et al. Arm and shoulder morbidity in breast cancer patients after breast-conserving therapy versus mastectomy. Acta Oncol 2008;47:835–42.
[38] Verry H, Lord SJ, Martin A, et al. Effectiveness and cost-effectiveness of sentinel lymph node biopsy compared with axillary node dissection in patients with early-stage breast cancer: a decision model analysis. Br J Cancer 2012;106:1045–52.
[39] Kanis JA, Brazier JE, Stevenson M, et al. Treatment of established osteoporosis: a systematic review and cost-utility analysis. Health Technol Assess 2002;6:1–146.
[40] Classe JM, Baffert S, Sigal-Zafrani B, et al. Cost comparison of axillary sentinel lymph node detection and axillary lymphadenectomy in early breast cancer: a national study based on a prospective multi-institutional series of 985 patients 'on behalf of the Group of Surgeons from the French Unicancer Federation'. Ann Oncol 2012;23:1170–7.
[41] Perrier L, Nessah K, Morelle M, et al. Cost comparison of two surgical strategies in the treatment of breast cancer: sentinel lymph node biopsy versus axillary lymph node dissection. Int J Technol Assess Health Care 2004;20:449–54.